LEGO-inspired drug design: Discovery of novel fungal Plasma membrane H+-ATPase (Pma1) inhibitors from small molecule libraries: An introduction of HFSA-SBS_DOS-RD strategy in drug discovery.

Tung, Truong Thanh; Dao, Trong Tuan; Palmgren, Michael B.; Fuglsang, Anja T.; Christensen, Soeren B.; Nielsen, John.

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2017

ACS Chemistry for Life®

Meeting Updates

253rd American Chemical Society National Meeting & Exposition

April 2-6, 2017 • San Francisco, CA

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253rd American Chemical Society National Meeting & Exposition

TABLE OF CONTENTS

ACS OPERATIONS OFFICES

- **Grand Hyatt Hotel San Francisco, Sausalito:** 415-848-6227
- **Hilton San Francisco Union Square, Nob Hill 1:** 415-923-7550
- **Hotel Nikko San Francisco, Lincoln Boardroom:** 415-403-1813
- **InterContinental San Francisco, Mission Room:** 415-616-6576
- **Marriott Union Square, City Suite:** 415-398-8900 x7519
- **San Francisco Marriott Marquis, Willow:** 415-284-8053
- **San Francisco Marriott Marquis, Awards Office, Laurel:** 415-284-8013
- **Moscone Center, South Lobby:** 415-978-3600
- **Moscone Center/West Building, Lobby:** 415-348-4400
- **Parc 55 San Francisco, Davidson:** 415-403-6670
- **Park Central San Francisco, Press Room:** 415-618-6812

INFORMATION CONTACTS

- **Attendee Registration, Moscone Center, North Lobby**: 415-978-3609
- **Career Fair Information Center, Moscone Center, Halls B/C**: 415-978-3613
- **Exhibitor Registration, Moscone Center, South Lobby**: 415-978-3611
- **Finance Office - Moscone Center, Room 110**: 415-978-3608
- **Host Local Section Booth, Moscone Center, North Lower Lobby**: 415-978-3616
- **Housing Assistance, Moscone Center, North Lobby**: 415-978-3610
- **Member Services, Moscone Center, North Lobby**: 415-978-3615
- **Press Center, Moscone Center, South Lobby**: 415-978-3605
- **Shuttle Desk Moscone Center, Outside West Lobby**: 415-348-4406
- **Society Program Office, Mason Room**: 415-923-7551
- **Governance Office, Union Square 22**: 415-923-7549

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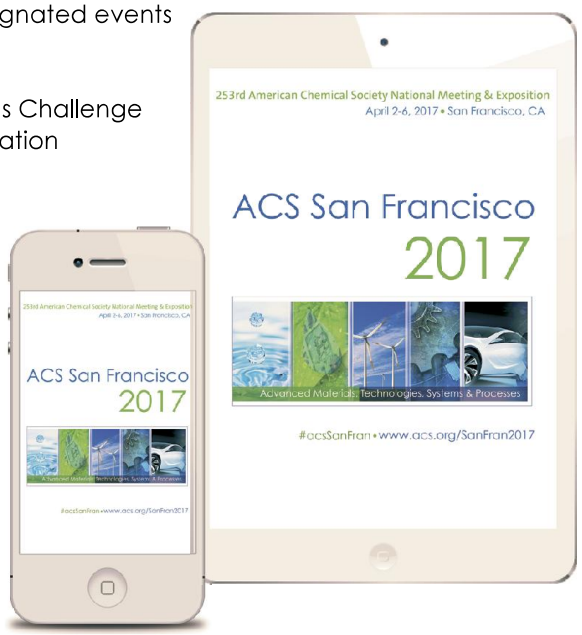
EMBRACING SUSTAINABILITY PRACTICES

The American Chemical Society continues to be a sustainability leader within the meeting and events community with most recently being the co-winner of the 2016 UFI Sustainable Development Award, 2016 RISE Award finalists, and the 2014 Trade Show Executive's Gold 100 Award as the show with the Most Commendable Green Initiatives. ACS and the Greener Meetings Program have also been showcased in Convene Magazine's August 2015 annual Best in Show issue for the "Best CSR Initiatives" and awarded the 2011 and 2012 PCMA Capital Chapter Green Leader Award.

Efforts of our sustainability practices are briefly noted below. These changes not only support a greener meeting but also improve your meeting experience.

- Condensed Onsite Program book with enhancing the mobile application and digital options
- Decreased print-run of the Onsite Program book due to digital and mobile applications
- Moved to using recycled paper for the Onsite Program Book
- Reformatted National Meeting website based on viewer analytics
- Free WiFi inside public areas at the Convention Center and many contracted hotels
- Established partnership with American Forests to offset carbon missions
- Audited contracted hotels on their sustainability efforts
- Partnered with Convention Center to source local foods for designated events
- Increased usage of digital signage
- Partnered with vendors that engaged in sustainability practices
- Increased attendee engagement through the Greener Meetings Challenge
- Adjusted meeting room temperature to 70° F for energy conservation



Thank you for your support in making ACS a leader in sustainability. Further information can be found at: www.acs.org/greenermeetings. There, you will find the ACS 2016 Sustainability Report including information on how to join the Greener Meetings Pledge.

Welcome to San Francisco and the 253rd ACS National Meeting

Welcome to beautiful San Francisco for the 253rd ACS National Meeting. It is my pleasure to join all of you in this vibrant city, and a favorite location for our meetings.

Advanced Materials, Technologies, Systems & Processes is the theme of this meeting. Twenty nine technical divisions and six committees are hosting original programming, including 1,100 half-day oral sessions and 144 poster sessions. More than 14,500 papers and nearly 5,700 posters will be presented at the meeting. In addition to symposia, there are a number of special events planned throughout the week.

Allison A. Campbell
ACS President

There are three Presidential Symposia that I encourage you to attend, as well as 14 symposia that I am recommending. Organized by the Division of Professional Relations, the LGBT Graduate & Postdoctoral Student Chemistry Research Symposium on Sunday and Monday will include scientific talks by LGBT graduate and postdoctoral students and a panel discussion on issues that affect LGBT students (Hotel Nikko San Francisco, Nikko Ballroom III). Sunday afternoon, Holy Grails in Chemistry: Celebrating the 50th Anniversary of Accounts of Chemical Research Journal will assess the progress made in critical areas of chemistry since first highlighted in a 1995 issue of the journal (San Francisco Marriott Marquis, Golden Gate A). On Monday, Science for a Sustainable Energy Future will focus on scientific advances in energy storage and chemical and biological approaches to energy conversion (Moscone Center, Room 133).

On Sunday afternoon, please join your colleagues at noon for the ACS Board of Directors Regular Session as we hear from two renown guest speakers: Joseph M. DeSimone presenting on the Future Fabricated with Light: The Launching of Carbon, and Anne Milasinic Andrews, talking about The Brain is More Than a Computer (Moscone Center, Gateway Ballroom 103/104).

On Monday afternoon, Bradley D. Olsen from the Massachusetts Institute of Technology will present the Kavli Foundation Emerging Leader in Chemistry Lecture on Classical challenges in the physical chemistry of polymer networks. Following his presentation, Jennifer A. Doudna of the University of California, Berkeley will give the Fred Kavli Innovations in Chemistry Lecture on CRISPR systems: Nature's toolkit for genome engineering (Moscone Center, Gateway Ballroom 103/104).

Throughout the meeting, many education-focused programs for high school teachers, undergraduate and graduate students, postdocs, and chemical professionals will be offered. For job seekers and employers, the career fair will feature on-site interviews, one-on-one career assistance, and workshops. Please find time to walk the expo hall where more than 400 booths will showcase services, instruments, books, and lab equipment of more than 250 companies.

My personal thanks to the members of the Santa Clara Valley Section and California Section; the divisional program chairs and symposium chairs responsible for organizing the technical sessions; and the ACS staff for making it all happen. Thanks to you for contributing to the success of this meeting, and of course for attending.

Allison A. Campbell
ACS President

Welcome Message from Kathryn Beers, San Francisco Thematic Program Chair

The Spring 2017 ACS National Meeting will be held April 2–6 in San Francisco, CA. The theme for the meeting is Advanced Materials, Technologies, Systems, and Processes.

Kathryn Beers
San Francisco Thematic Program Chair

The plenary session on Sunday afternoon, April 2, includes four invited lectures: Dr. Peter Green (National Renewable Energy Laboratory) will discuss "Clean energy challenge: An integrated approach involving basic research, innovation and human factors;" Dr. Jeffrey Linhardt (Verily Life Sciences) will discuss "Technology at the interface of microelectronics, life sciences, and big data: Materials challenges;" Dr. Ann-Christine Albertsson will discuss "From design and synthesis to advanced properties and sustainable polymeric materials;" Dr. Keith Watson (The Dow Chemical Company) will discuss "Fostering industrial and academic partnerships."

The Kavli Foundation Lecture Series will be held Monday, April 3. The Kavli Foundation Emerging Leader in Chemistry Lecture by Prof. Bradley Olsen (Massachusetts Institute of Technology) on "Classical challenges in the physical chemistry of polymer networks" and the Fred Kavli Innovations in Chemistry Lecture by Dr. Jennifer Doudna (UC Berkeley, Lawrence Berkeley National Lab) on "CRISPR systems: Nature's toolkit for genome engineering".

The technical program constructed by the ACS divisions includes 134 symposia that support the theme of the meeting. Divisions and committees with symposia supporting the theme include AGFD, ANYL, BIOT, CATL, CELL, CHED, CINF, COLL, COMP, ENFL, ENVR, HIST, I&EC, INOR, NUCL, ORGN, PHYS, PMSE, POLY, SCHB, and YCC. MPPG is cosponsoring a total of 27 symposia.

The program for the meeting and other information is available online at the website of the meeting, www.acs.org/sanfran2017.

I am very grateful to the members of the local section, the program chairs of the divisions and committees listed above, the thematic symposia chairs, and the ACS staff for their work in supporting the theme of this meeting. I look forward to meeting you in San Francisco!

Kathryn Beers
Thematic Program Chair

ACS Chemistry for Life®

Sunday, April 2, 2017
Noon-1:00 p.m.
Moscone Center
Gateway Ballroom 103/104 (Moscone South, Exhibit Level)

JOIN THE

ACS BOARD OF DIRECTORS REGULAR SESSION

AS THEY HOST "TED-TYPE TALKS" FEATURING GUEST SPEAKERS:

Joseph M. DeSimone, CEO/Co-founder of Carbon, Inc.; Chancellor's Eminent Professor of Chemistry, UNC-Chapel Hill; and William R. Kenan, Jr. Distinguished Professor of Chemical Engineering at NC State University and of Chemistry at UNC

"Future Fabricated with Light: The Launching of Carbon"

Joseph M. DeSimone has published over 300 scientific articles and has over 150 issued patents in his name with over 80 patents pending. In June 2016, DeSimone was recognized by President Barack Obama with the National Medal of Technology and Innovation. DeSimone is one of less than twenty individuals who have been elected to all three branches of the U.S. National Academies: National Academy of Medicine (2014), National Academy of Sciences (2012) and the National Academy of Engineering (2005).

DeSimone is the co-founder of several companies including Micell Technologies, Bioabsorbable Vascular Solutions, Liquidia Technologies and Carbon. DeSimone received his B.S. in Chemistry from Ursinus College in Collegeville, PA and his Ph.D. in Chemistry from Virginia Tech. He currently resides in Monte Sereno, California.

AND

Anne Milasincic Andrews, Professor of Psychiatry and Chemistry & Biochemistry; Semel Institute for Neuroscience & Human Behavior, Hatos Center for Neuropharmacology, and California NanoSystems Institute; University of California, Los Angeles

"The Brain is More Than a Computer"

Anne Milasincic Andrews leads efforts in basic and translational research on anxiety and depression, and at the nexus of nanoscience and neuroscience. Andrews' interdisciplinary research team focuses on understanding how the serotonin system and particularly, the serotonin transporter, modulate neurotransmission to influence complex behaviors including anxiety, mood, stress responsiveness, and learning and memory.

Andrews has been the recipient of an NIH Fellows Award for Research Excellence, an Eli Lily Outstanding Young Analytical Chemist Award, an American Parkinson's Disease Association Research Award, and a Brain and Behavior Research Foundation Independent Investigator Award. She is a member of the American College of Neuropsychopharmacology, International Society for Serotonin Research vice president, an advisory board member for the International Society for Monitoring Molecules in Neuroscience, and serves as Associate Editor for *ACS Chemical Neuroscience*.

Andrews earned her B.S. in chemistry from the Pennsylvania State University and received her Ph.D. in chemistry as a U.S. Department of Education Fellow working at the National Institute of Mental Health. There, she was also a postdoctoral fellow and senior staff fellow.

OFFICE OF THE GOVERNOR

April 2, 2017

American Chemical Society

On behalf of the State of California, I am pleased to welcome you to the 253rd American Chemical Society (ACS) National Meeting & Exposition.

Since its inception in 1876, the ACS has supported chemists and the chemical enterprise by providing professional and academic support to a growing network of members. Scientific research and emerging technologies continue to spur economic growth in California and in the broader global community. I commend all those who have come together to discuss the power of chemistry and I applaud your efforts to foster the innovators and innovations of tomorrow.

Best wishes for a memorable and productive meeting.

Sincerely,

EDMUND G. BROWN JR.

Office of the Mayor
City & County of San Francisco

Edwin M. Lee

GREETINGS FROM THE MAYOR OF SAN FRANCISCO

On behalf of the City and County of San Francisco, it is my pleasure to welcome you to the 253rd National Meeting of the American Chemical Society, focused on *Advanced Materials, Technologies, Systems and Processes*, held on April 2-6, 2017

The American Chemical Society (ACS) is the world's largest scientific society and one of the world's leading sources of authoritative scientific information. ACS is at the forefront of the evolving worldwide chemical enterprise and the premier professional home for chemists, chemical engineers and related professions around the globe.

San Francisco is proud to host this valuable event as our City continues to be a leader in scientific innovation, and we welcome the gathering of the brightest minds in the chemical sciences.

Congratulations to the American Chemical Society for their dynamic and visionary commitment to improving the lives of others through the transforming power of chemistry. I commend all the individuals who helped make this event a true success, and I wish you all the best in your future endeavors!

With warmest regards,

Edwin M. Lee
Mayor

1 Dr. Carlton B. Goodlett Place, Room 200, San Francisco, California 94102-4641
(415) 554-6141

9:30 MEDI **350.** Discovery of a novel class of potent, selective, and orally bioavailable histone methyltransferase Enhancer of Zeste Homolog 2 (EZH2) inhibitors and the identification of development candidate PF-06821497. **P. Kung**, S. Bergqvist, P. Bingham, J.F. Braganza, A. Brooun, M.R. Collins, W. Diehl, Y. Deng, D. Dinh, C. Fan, V.R. Fantin, H.J. Gukasyan, W. Hu, B. Huang, R. Kania, W. Liu, S. Kephart, M. Kraus, C. Krivacic, R.A. Kumpf, G. Li, K. Maegley, I.J. McAlpine, L. Nguyen, S. Ninkovic, M.A. Ornelas, D. Richter, E. Rui, M. Ryskin, S.A. Scales, J. Spangler, A. Stewart, S.C. Sutton, J. Tatlock, C. Tsao, D. Verhelle, F. Wang, H. Wang, P. Wells, M. Wythes, S. Yamazaki, B. Yip, X. Yu, L. Zehnder, W. Zhang, P. Zhu, J. Zhu, R.A. Rollins, S. Sharma, M.P. Edwards

10:00 MEDI **351.** Discovery and development of BLU-554: A potent, highly selective covalent inhibitor of Fibroblast Growth Factor Receptor 4 (FGFR4) in development for the targeted treatment of advanced Hepatocellular Carcinoma (HCC) patients with amplified and overexpressed FGF19. **C.V. Miduturu**, M. Hagel, M. Sheets, N. Rubin, W. Weng, N. Bifulco, L.V. Dipietro, J. Kim, N. Brooijmans, B.L. Hodous, N. Stransky, K. Hoeflich, V.J. Kadambi, N. Kohl, C. Lengauer, T. Guzi

10:30 MEDI **352.** Discovery of PRN1371: A highly selective, irreversible inhibitor of FGFR1-4 in clinical development for the treatment of solid tumors. **K.A. Brameld**

11:00 MEDI **353.** FGF401: A reversible-covalent inhibitor of FGFR4 for the treatment of hepatocellular carcinoma. **R.A. Fairhurst**, T. Knoepfel, P. Furet, N. Buschmann, C. Leblanc, R. Mah, M. Kiffe, D. Graus-Porta, A. Weiss, J. Kinyamu-Akunda, M. Wartmann, J. Trappe, T. Gabriel, F. Hofmann, W. Sellers

11:30 MEDI **354.** Interdiction at a protein-protein interface: Structure-based design of the Mcl-1 inhibitor AMG 176. **S.P. Brown**

Section B

Moscone Center

3006/3008

Targeting Epigenetic Writers & Erasers

J. Jin, *Organizer, Presiding*

8:30 Introductory Remarks.

8:35 MEDI **355.** Probing the epigenome for therapeutic targets. **C.H. Arrowsmith**

9:05 MEDI **356.** Tazemetostat, a first-in-class inhibitor of EZH2: From bench to bedside to bench. **R. Copeland**

9:35 MEDI **357.** Sirtuin inhibitors as promising anticancer agents. **H. Lin**

10:05 Intermission.

10:20 MEDI **358.** Targeting histone lysine methylation regulatory pathways in cancer. **P. Trojer**

10:50 MEDI **359.** Exploring novel models of interaction to inhibit protein methyltransferases. **M. Luo**

11:20 MEDI **360.** Chemical probes targeting the protein arginine deiminases. **P.R. Thompson**

11:50 Concluding Remarks.

WEDNESDAY AFTERNOON

Section A

Moscone Center

Gateway Ballroom 103/104

First Time Disclosures

J. B. Schwarz, *Organizer, Presiding*

1:30 MEDI **361.** Discovery of clinical candidate PF-06648671: A potent, highly brain penetrant gamma secretase modulator for the treatment of Alzheimer's disease. **M. Pettersson**, C. am Ende, T.W. Butler, P.H. Dorff, I.V. Efremov, E. Evrard, S.A. Eisenbeis, C.J. Helal, M.E. Green, J.M. Humphrey, G.W. Kauffman, P.B. Mullins, C.J. O'Donnell, D.A. Rankic, A.F. Stepan, C.M. Stiff, N. Patel, C. Subramanyam, T.P. Tran, E.X. Yang, L. Xie, K.R. Bales, E. Hajos-Korcsok, B.A. Pettersen, L.R. Pustilnik, S.J. Steyn, K.M. Wood, R. Qiu, P.R. Verhoest

2:00 MEDI **362.** Discovery of a small molecule αvβ6 inhibitor for idiopathic pulmonary fibrosis. **S.J. MacDonald**, J. Pritchard, N. Anderson

2:30 MEDI **363.** Identification of AZD9567, an anti-inflammatory glucocorticoid receptor modulator with improved side effect profile. **L. Ripa**, M. Dearman, G. Edenro, K. Edman, R. Hendrickx, M. Lepistö, L. Öberg

3:00 MEDI **364.** Discovery and early clinical profile of a non-catchol dopamine 1 receptor agonist. **D.L. Gray**, R. Kozak, S. Mente, J.E. Davoren, D. Nason, S. ONeil, I.V. Efremov, A. Harris, R. O'Connor, M. Salafia

3:30 MEDI **365.** Discovery and development of BLU-285: A potent, highly selective inhibitor of KIT and PDGFRα activation loop mutants. **B.L. Hodous**, E. Evans, A. Gardino, A. Davis, J. Zhu, D.P. Wilson, K. Wilson, L.V. Dipietro, J. Kim, N. Brooijmans, V.J. Kadambi, A. Shutes, Y. Zhang, N. Kohl, C. Lengauer, T. Guzi

4:00 MEDI **366.** NVP-LXS196, a novel PKC inhibitor for the treatment of uveal melanoma. **M. Visser**, J.P. Papillon, J. Fan, M. Luzzio, W. Michael, R. Wang, A. Zhang, C. Straub, S. Mathieu, M. Kato, M.G. Palermo, C. Chen, M.J. LaMarche, T.M. Ramsey, A. Vattay, R. Guo, V. Cooke, A. Bric, F. Chung, G. Liang, M. Romanowski, A. Wylie

4:30 MEDI **367.** Discovery of selonsertib (GS-4997): A first in class, selective inhibitor of apoptosis signal-regulating kinase 1. **G.T. Notte**, B. Corkey, E. Lansdon, D. Breckenridge, O.L. Saunders, M. Graupe, B. Murray, C. Venkataramani, J. Guerrero, J. Farand, J.A. Zablocki, K. Babaoglu, J. Liles, G. Budas, S. Wise, K. Koch, L. Castonguay, M.C. Desai

5:00 MEDI **368.** Discovery of a selective inhibitor of indoleamine-2,3-dioxygenase for use in the therapy of cancer. **A. Balog**

Section B

Moscone Center

3006/3008

General Orals

A. W. Stamford, *Organizer*

J. Ramanjulu, *Presiding*

1:30 MEDI **369.** Teaching old drugs new tricks: Reprogramming ethionamide's bioactivation to fight multidrug resistant *Mycobacterium tuberculosis*. **N. Willand**, M. Gitzinger, B. Deprez, A. Baulard

1:50 MEDI **370.** Preclinical development and characterization of MYC inhibitors. **N. Jacob**, P. Miranda, P. Serrano Navarro, J. Hart, P.K. Vogt, K.D. Janda

2:10 MEDI **371.** Discovery of PF-06748962: A potent and selective lactam-based EP3 antagonist. **K. Futatsugi**

2:30 MEDI **372.** Novel pyrrolomycins as potent antibacterial agents against *ESKAPE* pathogens and biofilms. **R. Li**, Z. Yang, J. Ahn, Y. Liu, Y. Chhonker, D. Murry, H.A. Zhong, K. Bayles

2:50 MEDI **373.** Development and application of an NMR-based activity and inhibition assay for mycobacterial isocitrate lyase. **R.P. Bhusal**, K. Patel, B. Kwai, G. Bashiri, J. Reynisson, J. Sperry, I.K. Leung

3:10 MEDI **374.** LEGO®-inspired drug design: Discovery of novel fungal Plasma membrane H^+-ATPase (Pma1) inhibitors from small molecule libraries: An introduction of HFSA-SBS_DOS-RD strategy in drug discovery. **T. Tung**, T. Dao, M.B. Palmgren, A.T. Fuglsang, S.B. Christensen, **J. Nielsen**

3:30 MEDI **375.** Reducing cycle time in medicinal chemistry drug discovery. **J.S. Wai**, T. Wang

3:50 MEDI **376.** Enzymatic tandem carboxylation-amidation as a bioactivity-potentiating strategy in the production of natural and unnatural thiolactomycin antibiotics. **J. Li**, X. Tang, S. Mckinnie, T. Awakawa, B.S. Moore

4:10 MEDI **377.** Structure-based design of highly potent small-molecule inhibitors of DCN1-UBC12 protein-protein interaction. **H. Zhou**, J. Lu, L. Liu, D. Bernard, J. Stuckey, Y. Sun, S. Wang

4:30 MEDI **378.** CDK8 inhibitors with long residence time emerging from a retro-design approach: New opportunities for cancer treatment. J.C. Benningshof, B. Aerts, **G. Müller**, J. Veerman, E. Damen, M. Kubbutat, J. Ehlert, H. Holger, F. Totzke

4:50 MEDI **379.** Structure-based design, synthesis, biological evaluation, and x-ray crystallographic analysis of novel, highly potent HIV-1 protease inhibitors to address multi-drug resistant HIV. A.K. Ghosh, **H.L. Osswald**, J. Agniswamy, Y. Wang, I. Weber, M. Amano, H. Mitsuya

WEDNESDAY EVENING

Section A

Moscone Center

West Hall

General Posters

A. W. Stamford, *Organizer*

7:00 - 9:00

MEDI **380.** Inhibition of Aβ-40 and Aβ-42 aggregation by piceatannol and cis-piceatannol. **J.M. Chapman**, M. Moss, Y. Wang

MEDI **381.** Photoelectrocatalytic inhibition of Alzheimer's β-amyloid aggregation in vitro by hole-derived radicals. **K. Kim**, B. Lee, Y. Chung, W. Choi

MEDI **382.** Synthesis of Yakuchinone-derived compounds that inhibit β-amyloid aggregation. **L. Chen**, C. Yen, H. Tseng, Y. Huang, Y. Lu, W. Hou, K. Hsu, I. Pan, K. Huang, W. Huang

MEDI **383.** Photoexcited ruthenium complex for highly sensitive inhibition of β-amyloidogenesis. **G. Son**, C. Park, B. Lee, Y. Chung

MEDI **384.** New hydroxyquinoline-based derivatives as potent modulators of amyloid-b aggregations. **M. Hu**

MEDI **385.** Potential multimechanistic therapeutic effects of dihydropyridine calcium channel blockers: Mechanistic study of effects on amyloid-beta aggregation associated with Alzheimer's disease. **J.M. Chapman**, M. Moss, J. Tseng

MEDI **386.** Withdrawn.

MEDI **387.** Development of MBRI-001, a deuterium-substituted plinabulin, as a potent anti-microtubule agent for anticancer. Z. Ding, H. Cheng, S. Wang, Y. Hou, J. Zhao, H. Guan, **W. Li**

MEDI **388.** β-Sheet propensity of competitive peptide inhibitor's residue is crucial in binding to proteases: PACE4 inhibitors as a case study. **V. Dianati**, A. Shamloo, A. Kwiatkowska, R. Desjardins, A. Soldera, R. Day, Y. Dory

MEDI **389.** Hepsin-targeted ligands for prostate cancer imaging and therapy. **Y. Byun**, S. Son, H. Kwon

MEDI **390.** X-ray crystallographic structures of teixobactin analogues. **H. Yang**, D.R. Du Bois, J.W. Ziller, J.S. Nowick

MEDI **391.** Withdrawn.

MEDI **392.** Long wavelength, orthogonal release of internalized anti-inflammatory compounds from cellular vehicles. **R.M. Hughes**, C. Marvin, Z. Rodgers, S. Ding, N. Oien, W.J. Smith, D.S. Lawrence

MEDI **393.** Amino acid and peptide conjugates are potential drug candidates. **S.S. Panda**

MEDI **394.** Withdrawn.

MEDI **395.** Directed immune responses via covalently linked TLR agonist combinations for a Q-fever vaccine. **T.J. Albin**, J. Tom, S. Manna, A. Gilkes, A. Jain, M. Supnet, H. Davies, A. Nalca, A. Burkhardt, P. Felgner, A.P. Esser-Kahn

MEDI **396.** Development of antidotes against nerve agent inhibited acetylcholinesterase – the transformation of an inhibitor into a reactivator. **C. Lindgren**, N. Forsgren, C. Akfur, L. Berg, D. Andersson, M. Hillgren, W. Qian, F. Worek, F. Ekström, A. Linusson

MEDI **397.** Generating site-specific antibody-drug conjugates with high drug to antibody ratios using a tandem Knoevenagel dondensation-Michael addition. **R. Kudirka**, R. Barfield, J. McFarland, P. Drake, A. Carlson, S. Banas, W. Zmolek, A. Garofalo, D. Rabuka

MEDI **398.** Synthesis of truncated tirandamycin A-D derivatives as new antihelminthic agents. **T. Jimenez**, M. Grotli, C. Wallentin

MEDI **399.** Beyond IC50 and simple PK models – considerations for discovery chemists. **R. Fraczkiewicz**, M.B. Bolger, W. Woltosz

MEDI **400.** Synthesis and evaluation of antitubercular agents 2-aminothiophenes and benzo-1,2-selenazol-3(2H)-ones targeting Pks13 and Ag85C respectively. **S. Thanna**, S.E. Knudson, C.M. Goins, F. Salem, S. Kapil, A. Grzegorzewicz, M. Jackson, D.R. Ronning, R.A. Slayden, S.J. Sucheck

‡ *Cooperative Cosponsorship*

MEDI **401.** Novel pyrimidine compounds as potent JAK inhibitors. **Y. Chen**, H. Li, R. Yen, T. Heckrodt, D. McMutrie, N. Lin, R. Singh, V. Taylor, M. Chan, E. Masuda, G. Park, D. Lau, D. Payan

MEDI **402.** Synthesis and evaluation polythiophene containing rhodamine dyes for biological and photochemical applications. **M.K. Linder**, J.N. Nasca, K.S. Gast, G. Sawada, D. Watson, M.R. Detty

MEDI **403.** Synthesis of β-configured clickable [^{18}F]FDGs as novel ^{18}F-fluoroglycosylation tools for PET *in vivo* imaging. **M. Elgland**, P. Nordeman, T. Fyrner, P. Konradsson, G. Antoni, P. Nilsson

MEDI **404.** Small-molecule anti-virulence agents for the prevention of dental biofilms. **B. Nijampatnam**, H. Wu, S.E. Velu

MEDI **405.** Discovery of novel pyrrolomycins as potential anticancer agents. **Y. Liu**, T. McGuire, Z. Yang, D. Coulter, Y. Chhonker, D. Murry, J. Sharp, H.A. Zhong, **R. Li**

MEDI **406.** Design and synthesis of small molecule inhibitors bearing 1,2,3-triazole/sulfonate pharmacophore from natural precursors for the treatment of bacterial infections. **B. Aneja**, S. Alam, M. Azam, A. Perwez, R. Haque, M. Rizvi, R. Maguire, K. Kavanagh, U. Yadava, C. Daniliuc, A. Azam, A. Mohammad

MEDI **407.** New N-substituted indazole-5-carboxamides as subnanomolar, selective monoamine oxidase B and dually active MAO-A/B inhibitors with BBB and GI permeability. **M. Gastreich**, C. Detering, L. Antonov, S. Hristova, H. Stammler, N.T. Tzvetkov

MEDI **408.** Withdrawn.

MEDI **409.** Glycosylated porphyrins for use in PET and PDT: Synthesis and characterization. **K. Arja**, M. Elgland, P. Nilsson

MEDI **410.** Selective nicotinic acetylcholine receptor activities from the areca nut. **N. Horenstein**, C. Stokes, R. Papke

MEDI **411.** Withdrawn.

MEDI **412.** Differentiating antiproliferative and chemopreventive modes of activity for electron-deficient aryl isothiocyanates against human MCF-7 cells. **J.R. Mays**

MEDI **413.** Application of the boronic acid as an isostere of the phenolic hydroxyl group in optimization of Selective Estrogen Receptor Downregulators (SERDs). **J. Liu**, S. Zheng, S. Guo, Q. Zhong, M. Bratton, T.E. Wiese, G. Wang

MEDI **414.** Withdrawn.

MEDI **415.** Substituted acylsulfonamides as surrogates of a terminal carboxylic acid: More effective small-molecule blockade of the Mcl-1 oncoprotein. **M.E. Lanning**, S. Fletcher

MEDI **416.** Novel class of substituted phenoxyacetamide derivatives as serotonin reuptake inhibitors and serotonin autoreceptor antagonists for repetitive behavior modulation in autism spectrum disorder. V.M. Gancarczyk, J. Dhuguru, A. Khalil, **O.M. Ghoneim**

MEDI **417.** Polymersomes for targeting and eradicating intracellular parasites. **L. Rizzello**, J. Robertson, P. M. Elks, T. McHugh, S. A. Renshaw, G. Battaglia

MEDI **418.** Two-in-one approach to modulate repetitive behaviors in autism spectrum disorder: N-arylpieprazines as key motifs towards developing bi-functional serotonergic ligands. **O.M. Ghoneim**

MEDI **419.** Zinc(II)-dipicolylamine coordination complexes are strongly active against cutaneous leishmaniasis. **M. Betancourt**, D. Rice, P. Vacchina, B. Norris-Mullins, M.A. Morales, B.D. Smith

MEDI **420.** Peptide-based nanosponges. **S.H. Bossmann**, H. Wang, A.S. Yapa, S.O. Wendel, N. Kariyawasam, T.B. Shrestha, M. Pyle, P.E. Smith, D.L. Troyer

MEDI **421.** Heterocyclic mimetics of crinine alkaloids – Novel scaffolds against drug-resistant cancer cells. **L.V. Frolova**

MEDI **422.** Characterization of histone lysine methyltransferase and discovery of NSD2 inhibitors. **J. Kwiatkowski**, A. Hung, Y. Tan, N. Ahmad, G. Lin, A. Ngo, Y. Li, H. Ng, J. Wee, X. Koh-Stenta, P.Z. Kwek, E.H. Ong, J.K. Joy, A. Poulsen, C. Kang, J. Hill, T.H. Keller

MEDI **423.** Computational rationalisation of ligand specific T-cell activation by the lipid presenting proteins CD1b and CD1c: Different means to the same end? **C. Cave-Ayland**, A. Chancellor, I. Tews, S. Mansour, C. Skylaris, J.W. Essex

MEDI **424.** Pharmacophore construction of Cyclooxygenase-2 (COX-2) selective inhibitors based on QSAR models. R.A. Gomes, G.L. Luiz Genesi, V.G. Maltarollo, **G.H. Trossini**

MEDI **425.** Perturbing dissimilar biomolecular targets from natural product scaffolds and focused chemical decoration. **J. Nielsen**, **T. Tung**, T. Holm Jakobsen, T. Dao, A.T. Fuglsang, M. Givskov, S.B. Christensen

MEDI **426.** Design of novel GPCR family-targeted scaffolds: Synthetic and cheminformatic exploration of novel medicinal chemistry space. **J.C. Benningshof**, G. Müller, T. Berkenbosch, D. Stumpfe, J. Bajorath

MEDI **427.** Synthesis and biological evaluation of C24 20S(OH)D3 analogs as anti-inflammatory agents. **Z. Lin**, S. Marepally, E. Goh, C.Y. Cheng, A.E. Postlethwaite, Z. Janjetovic, T. Kim, A.J. Slominski, R.C. Tuckey, N. Rochel, D.D. Miller, W. Li

MEDI **428.** Multi-omic approach to unraveling the microbial ecology of *Euphorbia* plant latex. M. Gunawardana, E. Hyde, S. Rivera, S. Webster, A. Castonguay, M. Anderson, S. Lahmeyer, B. Dorsey, T. La Val, D. VanderVelde, P. Webster, R. Knight, **M.M. Baum**

MEDI **429.** Discovery of novel indolinone derivatives as potent MELK inhibitors. **R. Edupuganti**, J.M. Taliaferro, Q. Wang, X. Xie, E.J. Cho, V. Sharma, P. Ren, C. Bartholomeusz, E.V. Anslyn, K.N. Dalby

MEDI **430.** Sphingosine analogues as inhibitors of Sphingosine Kinase (SK1). A. Cardona, M. Escudero-Casao, M. Corro, J. Hernandez, Y. Diaz, I. Matheu, S. Garcia-Vallve, M. Mulero, G. Pujadas, **S. Castillon**

MEDI **431.** Biological screening of *Moringa oleifera* for cytotocixity and antitumor activities. **E.P. Rodriguez**, C.A. Ospina

MEDI **432.** Design of a nucleic acid aptamer to achieve localization of a ROS-activated anti-cancer agent. **K.G. Earnest**, E.J. Merino

MEDI **433.** Exploring the binding site of GPR119 receptor inverse agonists. **E. Kotsikorou**, **S. Kowalski**

MEDI **434.** Methicillin-resistant *Staphylococcus aureus* becomes vulnerable to β-lactam antibiotics when in combination with branched polyethylenimine. **M. Foxley**, M. Xiao, S. Wright, S. Strange, A. Lam, K. Grogan, C.V. Rice

MEDI **435.** Old and new privileged scaffolds for medicinal chemistry. **P. Schneider**, G. Schneider

MEDI **436.** Vienna LiverTox Workspace: Towards predicting liver toxicity. **F. Montanari**, E. Kotsampasakou, B. Knasmüller, M. Pinto, M. Grandits, L. Richter, G.F. Ecker

MEDI **437.** Pyrrole-based antitubulin agents at the colchicine site: SAR of C-5 analogues in explicitly solvated models. **A.J. Obaidullah**, C.C. Rohena, J.A. Sikorski, S. Mooberry, J.T. Gupton, G.E. Kellogg

MEDI **438.** Design, synthesis, and biological evaluation of small molecule Giα2-androgen inhibitors in prostate cancer therapy. **S. Tapadar**, S. Caggia, S. Khan, A.K. Oyelere

MEDI **439.** Synthesis of GRB2 SH2 domain inhibitors: Analogues of sclerotiorin. **J.J. Gladfelder**, C. Arpin

MEDI **440.** Phytoestrogens: New ligands targeting the estrogen receptor domains. **V.J. Thakor**, M. Noolvi

MEDI **441.** Structure-based design of macrocyclic tetrapeptides intended to modulate the opioid receptors. **M.J. Ferracane**, J.V. Aldrich

MEDI **442.** MOEsaic: Making SAR analysis easier through the use of matched molecular pairs and R-group profiling. **A. Ajamian**

MEDI **443.** In search of AKT inhibitors as anticancer agents, an in silico approach. **P.J. Trejo**, A. Hernandez Campos, A. Romo-Mancillas, J.L. Medina-Franco, R. Castillo-Bocanegra

MEDI **444.** Design, synthesis and biological evaluation of Liver X Receptor (LXR) ligands. **R. Komati**, K.M. Lamark, K.A. Payne, M. Ndukwe, D. Spadoni, J. Sridhar, K. Riley

MEDI **445.** Amido phthalimides as CDKs and VEGF inhibitors. **R. Komati**, V.C. Miles, M. Ismail, F. Joseph, H. McFerrin, J. Sridhar

MEDI **446.** Withdrawn.

MEDI **447.** Discovery of Lu AF64196 a highly ligand efficient, brain penetrant and selective PDE1 inhibitor. **L.K. Rasmussen**, M. Langgard, C.T. Christoffersen, J. Nielsen, C. Bundgaard, J. Kehler

MEDI **448.** Repurposing for G-protein couple receptors by structure-based discovery: Transformation of adenosine derivatives into $5HT_{2B}$/$5HT_{2C}$ serotonin receptor antagonists. **D. Tosh**, A. Ciancetta, E.P. Warnick, S. Crane, Z. Gao, K.A. Jacobson

MEDI **449.** Discovery of highly selective Itk inhibitors with *in vivo* IL-2 inhibition. **S. Takai**, H. Takeda, A. Watanabe, K. Tsuboi, R. Suzuki, A. Hiramatsu, Y. Iyoda, T. Inukai, A. Kinoshita, H. Kohno, B. Liu, R. Shetty, K. Moriarty, M. Kurono, S. Umemura, H. Egashira, J. Zou, Z. Konteatis, R. Omi, H. Namboodiri, W. Sawada, M. Murata, T. Koike, R. Komaki-Nishikawa, N. Yada, T. Yoshizawa, J. McCool, M. Bukhtiyarova, M. Kelly, J. Takeuchi

MEDI **450.** Decoupling proton motive force to overcome antibacterial resistance. **J. Buonomo**, C.C. Aldrich

MEDI **451.** Adverse drug reactions triggered by the common HLA-B*57:01 variant: Virtual screening of DrugBank. **G. Van Den Driessche**, D. Fourches

MEDI **452.** Optimization of 4(1*H*)-quinolone antimalarials for oral bioavailability and in vivo efficacy. **C. Lichorowic**, J.R. Maignan, R. Neelarapu, A. Monastyrski, J.V. Giarrusso, T. Mutka, L. Blake, D. Casandra, A. LaCrue, D. Kyle, R. Manetsch

MEDI **453.** Design of inhibitors for the human papillomavirus E6 protein. **D.P. Petrov**, V.J. Davisson, E. Androphy, A. Rietz

MEDI **454.** Scaffold replacement and 3D ligand optimization applied to the discovery of tyrosine kinase inhibitors. **A. Deschenes**

MEDI **455.** Discovery of the first low-molecular-weight *Mycobacterium tuberculosis* MabA (FabG1) inhibitors using a fragment-based approach. C. Pintilala, M. Moune, K. Bourbiaux, R. Frita, K. Djaout, C. Piveteau, B. Deprez, A. Baulard, N. Willand, **M. Flipo**

MEDI **456.** Structure-based, in molecular design and synthesis of inhibitors of protein kinase family of receptors of epidermal growth factor. **A.S. Bunev**, E.V. Sukhonosova, G. Lisnik, N. Yabbarov, G. Ostapenko

MEDI **457.** *In vivo* structure-efficacy studies of regioisomeric artero-lane-like endoperoxides. **B.R. Blank**, J. Gut, P.J. Rosenthal, A.R. Renslo

MEDI **458.** Optimization of peptide substrates for conjugate modification of macromolecular mediated RNAi delivery. **J.C. Carlson**, J. Benson, A.V. Blokhin, D. Rozema, A. Sokoloff

MEDI **459.** Impact of activation of GPR68 by metal cations on high throughput screening. **C. Wang**, S. Lin, L.D. Fader, A. Granger

MEDI **460.** Synthesis of 1,2,4-substituted imidazoles for a fragment-based drug discovery library. **T. Lafferty**, J. Patrone

MEDI **461.** Identification and optimization of 5-aryl benzimidazolones as AMPA receptor negative modulators selective for TARP-γ8. **S. Ravula**, **M. Ameriks**, **B.M. Savall**, **J.M. Ziff**, **B.T. Shireman**, **M.J. Seierstad**, **N. Wu**, **B. Lord**, **M. Maher**, **N.I. Carruthers**, **T.W. Lovenberg**

MEDI **462.** Design and synthesis of L-neplanocin analogues as antiviral agents. **Q. Chen**, C. Liu, S. Schneller, **A. Davidson**, **M. Stout**